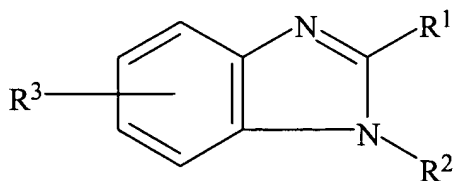


I. AMENDMENT

Listing of the Claims

The following listing of the claims replaces all previous listings or version of the claims:

1. (Original) A method for inducing apoptosis in a cell expressing a tumor suppressor gene comprising administering an effective amount of a benzimidazole to said cell, wherein the expression of the tumor suppressor gene by the cell and the benzimidazole results in the apoptosis of the cell.
2. (Original) The method of claim 1, wherein the benzimidazole is a derivative having the formula:



wherein R³ is selected from the group consisting of H, carboxyl (-CO₂H), hydroxyl, amino, chloro, difluoromethoxy, benzoyl, phenyl-thio, pyridinyl, propyl-thio, diphenyl, methoxy(methoxy-dimethyl,pyridinyl)methyl-(sulfonyl), fluorophenylmethyl-2-chloro, propenyl, chloropropyl or esters (-CO₂R⁴) wherein R⁴ is selected from the group consisting of alkoxy, haloalkyl, alkenyl, and cycloalkyl, wherein the alkyl groups have from 1 – 8 carbons, or CH₃CH₂(OCH₂CH₂)_n—, or CH₃CH₂CH₂(OCH₂CH₂CH₂)_n—, or (CH₃)₂CH(OCH(CH₃)CH₂)_n—, wherein n is from 1 – 3, wherein R¹ is OH, Cl, SH, carbamate or piperidin-4-yl, and R² is hydrogen, α-methylvinyl, 3-chloropropyl or piperidin-4-yl, or the pharmaceutically effective organic or inorganic salts thereof, or mixtures thereof.

3. (Original) The method of claim 2, wherein the benzimidazole derivative is methyl 5-benzoylbenzimidazole-2-carbamate (mebendazole).

9. (Original) The method of claim 1, wherein the dose of benzimidazole is at least 0.05 µg/ml.
10. (Original) The method of claim 1, wherein benzimidazole administration is repeated at least once.
12. (Original) The method of claim 1, wherein the cell is a tumor cell.
13. (Original) The method of claim 12, wherein the tumor cell is a multidrug resistant tumor cell.
14. (Original) The method of claim 13, wherein the multidrug resistant tumor cell is a lung tumor cell, a non-small cell lung carcinoma cell, a breast cancer cell, or a sarcoma cell.
15. (Original) The method of claim 12, wherein the tumor cell is a lung tumor cell.
16. (Original) The method of claim 15, wherein the lung tumor cell is a non-small cell lung carcinoma cell.
17. (Original) The method of claim 12, wherein the tumor cell is a breast cancer cell.
18. (Original) The method of claim 12, wherein the tumor cell is a sarcoma cell.
19. (Original) The method of claim 12, wherein the tumor suppressor gene is *p53*, *p16*, *p21*, *Rb*, *p15*, *BRCA1*, *BRCA2*, *zac1*, *p73*, *ATM*, *HIC-1*, *DPC-4*, *FHIT*, *NF2*,

APC, DCC, PTEN, ING1, NOEY1, NOEY2, PML, OVCA1, MADR2, WT1, 53BP2, IRF-1, MDA-7 and C-CAM.

20. (Original) The method of claim 12, wherein the tumor suppressor gene is MDA-7.

21. (Original) The method of claim 12, wherein the tumor suppressor gene is *p53*.

22. (Previously Presented) The method of claim 12, further comprising the step of determining the tumor suppressor gene status of the tumor cell prior to the method of claim 1.

23. (Original) The method of claim 22, wherein determining comprises Southern blotting.

24. (Original) The method of claim 22, wherein determining comprises Northern blotting.

25. (Original) The method of claim 22, wherein determining comprises PCR.

26. (Original) The method of claim 22, wherein determining comprises ELISA.

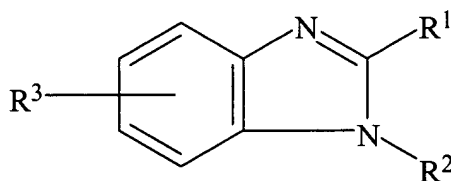
27. (Original) The method of claim 22, wherein determining comprises Western blotting.

28. (Original) The method of claim 22, wherein determining comprises immunofluorescence.

29. (Original) The method of claim 12, wherein the tumor cell expresses a functional tumor suppressor gene.

75. (Original) A method for treating a patient having cancer, wherein cancer cells express a tumor suppressor, comprising administering an effective amount of a benzimidazole to said patient, wherein the expression of the tumor suppressor gene by the cancer cell and the administration of the benzimidazole results in the inhibition of said cancer.

76. (Original) The method of claim 75, wherein the benzimidazole is a derivative having the formula:



wherein R^3 is selected from the group consisting of H, carboxyl ($-\text{CO}_2\text{H}$), hydroxyl, amino, chloro, difluoromethoxy, benzoyl, phenyl-thio, pyridinyl, propyl-thio, diphenyl, methoxy(methoxy-dimethyl,pyridinyl)methyl-(sulfonyl), fluorophenylmethyl-2-chloro, propenyl, chloropropyl or esters ($-\text{CO}_2\text{R}^4$) wherein R^4 is selected from the group consisting of alkoxy, haloalkyl, alkenyl, and cycloalkyl, wherein the alkyl groups have from 1 – 8 carbons, or $\text{CH}_3\text{CH}_2(\text{OCH}_2\text{CH}_2)_n-$, or $\text{CH}_3\text{CH}_2\text{CH}_2(\text{OCH}_2\text{CH}_2\text{CH}_2)_n-$, or $(\text{CH}_3)_2\text{CH}(\text{OCH}(\text{CH}_3)\text{CH}_2)_n-$, wherein n is from 1 – 3, wherein R^1 is OH, Cl, SH, carbamate or piperidin-4-yl, and R^2 is hydrogen, α -methylvinyl, 3-chloropropyl or piperidin-4-yl, or the pharmaceutically effective organic or inorganic salts thereof, or mixtures thereof.

77. (Original) The method of claim 75, wherein the benzimidazole derivative is methyl 5-benzoylbenzimidazole-2-carbamate (mebendazole).

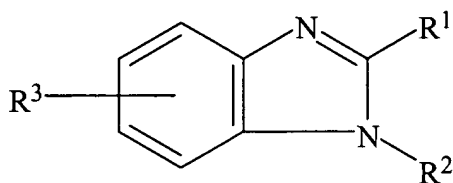
83. (Original) The method of claim 75, wherein the tumor suppressor gene is *p53*, *p16*, *p21*, *Rb*, *p15*, *BRCA1*, *BRCA2*, *zac1*, *p73*, *ATM*, *HIC-1*, *DPC-4*, *FHIT*, *NF2*, *APC*, *DCC*, *PTEN*, *ING1*, *NOEY1*, *NOEY2*, *PML*, *OVCA1*, *MADR2*, *WT1*, *53BP2*, *IRF-1*, *MDA-7* and *C-CAM*.

84. (Original) The method of claim 75, wherein the tumor suppressor gene is MDA-7.
85. (Original) The method of claim 75, wherein the tumor suppressor gene is *p53*.
86. (Original) The method of claim 75, wherein the cancer cell is a multidrug resistant tumor cell.
87. (Original) The method of claim 86, wherein the multidrug resistant tumor cell is a lung tumor cell, a non-small cell lung carcinoma cell, a breast cancer cell, or a sarcoma cell.
88. (Original) The method of claim 75, wherein the cancer cell is a lung tumor cell.
89. (Original) The method of claim 88, wherein the lung tumor cell is a non-small cell lung carcinoma cell.
90. (Original) The method of claim 75, wherein the cancer cell is a breast cancer cell.
91. (Original) The method of claim 75, wherein the cancer cell is a sarcoma cell.
92. (Original) The method of claim 75, wherein benzimidazole administration comprises intratumoral administration.
93. (Original) The method of claim 75, wherein benzimidazole administration comprises systemic administration.
94. (Original) The method of claim 75, wherein benzimidazole administration comprises oral administration.

95. (Original) The method of claim 75, wherein benzimidazole administration comprises administration in the area local to a tumor in said patient.
96. (Original) The method of claim 75, wherein benzimidazole administration comprises administration in the area regional to a tumor in said patient.
97. (Original) The method of claim 75, wherein benzimidazole administration is repeated at least once.
98. (Original) The method of claim 75, wherein the dose of benzimidazole is about 0.1 mg per kg body weight.
99. (Original) The method of claim 75, wherein the dose of benzimidazole is about 1.0 mg per kg body weight.
100. (Previously Presented) The method of claim 83, further comprising the step of determining the tumor suppressor gene status of the cancer cell prior to the method of claim 75.
101. (Original) The method of claim 100, wherein determining comprises Southern blotting.
102. (Original) The method of claim 100, wherein determining comprises Northern blotting.
103. (Original) The method of claim 100, wherein determining comprises PCR.
104. (Original) The method of claim 100, wherein determining comprises ELISA.
105. (Original) The method of claim 100, wherein determining comprises Western blotting.

106. (Original) The method of claim 100, wherein determining comprises immunofluorescence.

161. (Currently Amended) A method for treating a patient with a hyperproliferative disorder comprising administering to said subject an amount of a benzimidazole effective to induce apoptosis of a cell in said patient, wherein the benzimidazole is a derivative having the formula:



wherein R³ is selected from the group consisting of H, carboxyl (-CO₂H), hydroxyl, amino, chloro, difluoromethoxy, benzoyl, phenyl-thio, pyridinyl, propyl-thio, diphenyl, methoxy(methoxy-dimethyl,pyridinyl)methyl-(sulfonyl), fluorophenylmethyl-2-chloro, propenyl, chloroprophyl or esters (-CO₂R⁴) wherein R⁴ is selected from the group consisting of alkoxy, haloalkyl, alkenyl, and cycloalkyl, wherein the alkyl groups have from 1 – 8 carbons, or CH₃CH₂(OCH₂CH₂)_n—, or CH₃CH₂CH₂(OCH₂CH₂CH₂)_n—, or (CH₃)₂CH(OCH(CH₃)CH₂)_n—, wherein n is from 1 – 3,

wherein R¹ is OH, Cl, SH, carbamate or piperidin-4-yl,

wherein R² is hydrogen, α-methylvinyl, 3-chloropropyl or piperidin-4-yl,

wherein if R³ is H or chloro, then R² cannot be H if R¹ is carbamate,

or the pharmaceutically effective organic or inorganic salts thereof, or mixtures thereof.

162. (Currently Amended) The method of claim 161, wherein said subject patient suffers from cancer.

164. (Canceled)

165. (Canceled)

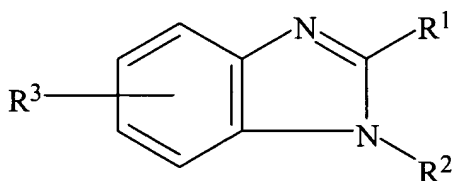
167. (Canceled)

169. (Canceled)

170. (Canceled)

176-182. (Canceled)

183. (New) The method of claim 1, wherein the benzimidazole is a derivative having the formula:



wherein R³ is selected from the group consisting of H, carboxyl (-CO₂H), hydroxyl, amino, chloro, difluormethoxy, benzoyl, phenyl-thio, pyridinyl, propyl-thio, diphenyl, methoxy(methoxy-dimethyl,pyridinyl)methyl-(sulfonyl), fluorophenylmethyl-2-chloro, propenyl, chloroprophyl or esters (-CO₂R⁴) wherein R⁴ is selected from the group consisting of alkoxy, haloalkyl, alkenyl, and cycloalkyl, wherein the alkyl groups have from 1 – 8 carbons, or CH₃CH₂(OCH₂CH₂)_n—, or CH₃CH₂CH₂(OCH₂CH₂CH₂)_n—, or (CH₃)₂CH(OCH(CH₃)CH₂)_n—, wherein n is from 1 – 3,

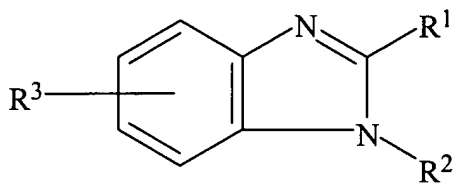
wherein R¹ is OH, Cl, SH, carbamate or piperidin-4-yl,

wherein R² is hydrogen, α-methylvinyl, 3-chloropropyl or piperidin-4-yl,

wherein if R³ is H or chloro, then R² cannot be H if R¹ is carbamate,

or the pharmaceutically effective organic or inorganic salts thereof, or mixtures thereof.

184. (New) The method of claim 75, wherein the benzimidazole is a derivative having the formula:



wherein R^3 is selected from the group consisting of H, carboxyl ($-\text{CO}_2\text{H}$), hydroxyl, amino, chloro, difluormethoxy, benzoyl, phenyl-thio, pyridinyl, propyl-thio, diphenyl, methoxy(methoxy-dimethyl,pyridinyl)methyl-(sulfonyl), fluorophenylmethyl-2-chloro, propenyl, chloropropyl or esters ($-\text{CO}_2R^4$) wherein R^4 is selected from the group consisting of alkoxy, haloalkyl, alkenyl, and cycloalkyl, wherein the alkyl groups have from 1 – 8 carbons, or $\text{CH}_3\text{CH}_2(\text{OCH}_2\text{CH}_2)_n-$, or $\text{CH}_3\text{CH}_2\text{CH}_2(\text{OCH}_2\text{CH}_2\text{CH}_2)_n-$, or $(\text{CH}_3)_2\text{CH}(\text{OCH}(\text{CH}_3)\text{CH}_2)_n-$, wherein n is from 1 – 3,

wherein R^1 is OH, Cl, SH, carbamate or piperidin-4-yl,

wherein R^2 is hydrogen, α -methylvinyl, 3-chloropropyl or piperidin-4-yl,

wherein if R^3 is H or chloro, then R^2 cannot be H if R^1 is carbamate,

or the pharmaceutically effective organic or inorganic salts thereof, or mixtures thereof.

II. RESPONSE TO OFFICE ACTION

A. Status of the Claims

Claims 1-29, 75-77, 83-106, 161 and 162 are currently under consideration. Claims 4-8, 11, 30-74, 78-82, 107-160, 163, 166, 168 and 171-175 have been previously withdrawn from consideration as being drawn to a non-elected invention and/or species. Claims 164, 165, 167, 169-170, and 176-182 have been previously canceled without prejudice or disclaimer.

Claims 161 and 162 have been amended in the Amendment set forth herein. Claim 161 has been amended to recite certain structural features of benzimidazoles. Support for the amendment to claim 161 can be found generally throughout the specification, such as on page 8, line 22 through page 9, line 13. Claim 162, which depends from claim 161, has been amended to recite “patient” instead of “subject” since claim 161 recites “patient.” Exemplary support for “patient” can be found on page 4, lines 8-10, and in claim 162.

New claims 183-184 have been added. Written description support for the structural limitations in the new claims (as well as in amended claim 161) can be found throughout the specification, such as on page 8, line 5 through page 9, line 22. Additional detail regarding written description support is discussed in the response below.